12. TOXICOLOGY

NAME	SCHOOL	E-MAIL
Gary O. Rankin Chairman	Marshall University	rankin@marshall.edu
Paul Hollenberg	University of Michigan	phollen@UMICH.edu
I. Glenn Sipes	University of Arizona	sipes@email.arizona.edu
James R. Halpert	UT Medical Branch– Galveston	jhalpert@utmb.edu
Jaime Matta	Ponce School of Medicine	jmatta@psm.edu
David Hein	University of Louisville	d.hein@louisville.edu

TOXICOLOGY AND THERAPY OF INTOXICATION (5.0 hr)

Introduction

A medical pharmacology course should be primarily concerned with three aspects of toxicology: adverse effects of therapeutic agents, acute intoxications, and chronic poisoning/environmental toxicology. The adverse effects of drugs should be taught along with the pharmacology of individual drugs or groups of drugs.

The discussion of acute intoxications should constitute a short, but important, part of the pharmacology course and should deal with the techniques and procedures used in dealing with the effects of exposure to acutely toxic materials. Lectures dealing with chronic intoxications should emphasize environmental toxicology and risk assessment.

Major recommendations:

1. **Principles of Toxicology**: Many of the mechanisms by which chemicals induce toxic effects are governed by the same principles (e.g. pharmacodynamics, pharmacokinetics) that govern pharmacological effects. The principles section of the pharmacology course could cover both of these topics. The principles of toxicology section can be presented with some additional time to cover bioactivation, cellular defense mechanisms, and threshold concepts. Moreover, these principles should be reinforced and reiterated later in the toxicology section of the course. (1 hr)
2. **Toxicology of Individual Drugs and Drug Groups**: The toxicological effects of drugs should be included in the discussion of the pharmacology of the specific drugs and drug groups. A discussion of the toxicology of heroin and other opiates, cocaine, and cardiac glycosides, for example, provides an opportunity to relate principles of toxicology to the therapy of intoxication.
3. **Priority Toxic Chemicals**: Rather than extensive discussions of many individual toxicants, priority should be given to select chemicals to include acetaminophen, tricyclic antidepressants**,** carbon monoxide, cyanide, lead, iron (if not discussed

elsewhere), methanol (if not discussed along with ethanol and other alcohols in the CNS section of the course)**,** and organophosphate and carbamate pesticides (if not discussed in the ANS section of the course). This list may be expanded in some schools to satisfy perceived local or regional needs. For example, agricultural chemicals may be given more emphasis in rural areas and air pollutants may be emphasized in urban areas. Finally, the therapeutic use of specific antidotes could be covered along with the relevant priority chemicals or could be discussed in connection with the management of intoxication. (2 hr)

4. **Management of Acute Intoxications**: The therapeutic approach to the management of acute intoxication with either drug or non-drug chemicals should be taught. This lecture could effectively present a "decision-tree" approach. If the identity of the poison is known, then the approach would be different than in the case where the identity of the poison is not known. A discussion of the hepatotoxicity of acetaminophen affords an opportunity to relate bioactivation mechanisms, the protective role of glutathione, and therapy with N-acetylcysteine in a case-based setting.
5. **Environmental Toxicology/Risk Assessment**: Because chronic, low-dose exposures to chemicals occur more frequently than acute, high-dose exposures, medical students should be provided with information about risk assessment and the hazard**s** associated with chronic exposure to chemicals. Moreover, chronic use of therapeutic agents at moderately high doses, compared to low dose exposure to chemicals in the food, air and water, is now commonplace.

   Lectures in this area should deal with the neurotoxic, carcinogenic, mutagenic, and teratogenic potential of chemicals including:

   a. Carcinogenic (e.g., the concept of precarcinogen, proximate and ultimate carcinogen.
   b. Metabolic transformations of chemical carcinogens.
   c. Mechanisms of carcinogenesis (initiation and promotion processes, relationship with DNA binding, concept of DNA repair).
   d. Mutagenicity and relationships with carcinogenicity, Ames test.
   e. Smoking and lung cancer (if not covered adequately in pathology) e.g., major carcinogens in cigarette smoke.
   f. Chemical prevention of carcinogenicity (e.g. antioxidants).
   g. Neurotoxic potential as a common basis for establishing exposure limits.

   These lectures provide an excellent opportunity to reinforce fundamental concepts (dose-response, variability of responses in a population, etc.) and to train students to use these concepts in evaluating risk. The reliance on fundamental concepts is important in an area where reliable data for the human population is usually lacking.

6. **Sources of Information**: Because intoxication associated with diverse types of chemicals may be encountered in clinical practice, medical students should be aware of the information sources available to them. A presentation by the Director

of the local or regional poison information center may be effective. Students should also be made aware of available CD-ROM or Internet databases on toxicants. (2 hr for 4, 5 and 6)

7. **Lecture Time:** In the idealized curriculum, about five lectures should be devoted to toxicology. These lectures may be held in conjunction with discussions in clinical conferences.

Specific knowledge objectives to be considered:

1. Describe four basic components in the management of acute poisoning (evaluation of the poisoned individual, supporting care, termination of exposure, and specific drug therapy) and how to decide on their sequence of initiation.
2. Describe a Poison Control Center and list services a physician should expect from an ideal center. Provide information concerning current Internet sources of toxicology databases.
3. Discuss the general principles of risk assessment associated with long-term, low dose exposures. How can fundamental concepts (i.e. dose-response) be used in assessing risk**?**